CLAIMS

1. A method for rapid crystallization of biomolecules, comprising:
   (a) providing at least one biomolecule species;
   (b) providing at least one crystallization reactor comprising an IEF buffer having a pH range, the pH range encompassing the pI of the at least one biomolecule species;
   (c) bringing said at least one biomolecule species into contact with the at least one crystallization reactor;
   (d) introducing an electric field at said at least one crystallization reactor thereby generating a concentrated solution of said at least one biomolecule species; and
   (e) obtaining at least one crystal within said at least one crystallization reactor.

2. The method according to claim 1, wherein step (c) further comprises depositing the at least one crystallization reactor and the at least one biomolecule species in running buffer.

3. The method according to claim 2, further comprising stirring the running buffer.

4. The method according to claim 1, wherein step (e) further comprises monitoring the formation of a biomolecule crystal.

5. The method according to any one of claims 1-4 wherein the crystallization occurs within 24 hours, preferably within less than 12 hours.

6. The method according to claim 1, wherein the at least one biomolecule species is selected from the group consisting of: peptides, proteins, polypeptides, enzymes, antibodies, protein-DNA complexes, protein complexes comprising chemical entities, polynucleotides, DNA, RNA, antigens, antigenic epitopes and variants thereof, hormones, carbohydrates, lipids, phospholipids and biotinylated probes.

7. The method according to claim 6, wherein the biomolecule species is selected from a polypeptide or a protein.

8. The method according to claim 1, wherein the at least one biomolecule species in step (a) is immobilized onto a substrate.

9. The method according to claim 1, wherein the at least one crystallization reactor is provided within a capillary.

10. The method according to claim 1, wherein the at least one crystallization reactor is linked, joined, or substantially contiguous to a solid substrate.

11. The method according to claim 1, wherein the IEF buffer further comprises a polymer.

12. The method according to claim 11, wherein the polymer is selected from the group consisting of: linear polymers, branched polymers, polyacrylamide, agarose, hydrogels, cellulose, modified cellulose, cross-linked polyvinyl alcohol, cross-linked polyethylene oxide and glycol polymer.

13. The method according to claim 11, wherein the at least one crystallization reactor has a cylindrical form.

14. The method according to claim 13, wherein the cylindrical form has a diameter from about 20 μm to about 10 mm and a length from about 0.5 mm to about 10 mm.

15. The method according to claim 1, wherein the IEF buffer has a pH range of no more than 0.2 pH units.

16. The method according to claim 15, wherein the IEF buffer has a pH range of no more than 0.02 pH units.

17. The method according to claim 2, wherein the temperature of the running buffer is maintained within the range of 0-30°C.

18. The method according to claim 17, wherein the electric field is maintained between 50 V/cm to 2000 V/cm.

19. The method according to claim 1, wherein the electric field is being supplied as DC or AC.

20. The method according to any one of claims 1 to 19, wherein in step (b) a plurality of crystallization reactors is provided, each crystallization reactor comprising an IEF buffer.

21. The method according to claim 20, wherein the IEF buffer has a pH range of no more than 0.2 pH units.

22. The method according to claim 21, wherein the IEF buffer has a pH range of no more than 0.02 pH units.

23. The method according to claim 20, wherein the IEF buffers in the plurality of crystallization reactors are different from one another.

24. The method according to claim 23, wherein the pH ranges of the plurality of IEF buffers partially overlap with one another.

25. The method according to claim 23, wherein the pH ranges do not overlap.

26. The method according to claim 25, wherein the pH step between one or more IEF buffers is no more than 0.1 pH units.

27. The method according to claim 26, wherein the pH step between one or more IEF buffers is no more than 0.02 pH units.

28. The method according to claim 20, wherein the crystallization reactors are isolated from one another.

29. The method according to claim 28, wherein the plurality of crystallization reactors are linked, joined, or substantially contiguous to a substrate.

30. The method according to claim 29, wherein the plurality of crystallization reactors are linked, joined, or substantially contiguous with a substrate in a spatially addressable manner.

31. The method according to claim 29, wherein the substrate is biomolecule impermeable.

32. The method according to claim 29, wherein the substrate is ion impermeable.

33. The method according to claim 29, wherein the plurality of crystallization reactors are linked, joined, or substantially contiguous to a substrate in an arrangement selected from the group consisting of: immobilized pH gradient strips, pH membranes and pre-cast gels.

34. The method according to claim 1, further comprising prior to step (a) the step of sorting a solution comprising at least one biomolecule species.

35. A method for sorting a solution comprising a plurality of biomolecules and rapidly crystallizing at least one biomolecule species, comprising:

(a) providing a medium comprising a plurality of biomolecules;

(b) sorting the plurality of biomolecules on a substrate, thereby obtaining at least one locus on the substrate comprising at least one biomolecule species;

(c) recovering a portion from said substrate, the portion comprising the at least one locus;

(d) providing at least one crystallization reactor comprising an IEF buffer having a pH range, the pH range encompassing the pI of the at least biomolecule;

(e) bringing the portion of (c) into contact with the at least one crystallization reactor;

(f) introducing an electric field at the at least one crystallization reactor thereby generating within said at least one crystallization reactor a concentrated solution of said at least one biomolecule species; and

(g) obtaining at least one crystal within said at least one crystallization reactor of (f).

36. The method according to claim 35, wherein step (b) is carried out by a method selected from the group consisting of: isoelectric focusing, thin layer chromatography, including High Performance Liquid Chromatography (HPLC) techniques, and gel electrophoresis.

37. The method according to claim 36, wherein the method is performed under non-denaturing conditions.

38. The method according to claim 35, wherein sorting in step (b) is by the mass of the at least one biomolecule species.

39. The method according to claim 35, wherein step (e) further comprises depositing said portion and the at least one crystallization reactor in running buffer.

40. The method according to claim 39, further comprising stirring the running buffer.

41. The method according to any one of claims 35 to 40, wherein the at least one biomolecule species is selected from a protein or a polypeptide.

42. The method according to any one of claims 35 to 41, wherein the crystals are obtained within 24 hours, preferably in less than 12 hours.

43. The method according to any one of claims 35 to 42, wherein the IEF buffer comprises a polymer.

44. The method according to claim 35, wherein the pH range spans no more than 0.2 pH units.

45. The method according to claim 35, wherein the temperature of the running buffer is maintained within the range of 0 to 30°C.

46. The method according to claim 45, wherein the electric field is between 50 V/cm to 2000 V/cm.

47. The method according to claims 35, wherein the electric field is being supplied as DC or AC.

48. The method according to claim 35, wherein the substrate in step (b) is a gel.

49. The method according to claim 35, wherein the substrate in step (b) comprises a polymer selected from the group consisting of: polyacrylamide, agarose, hydrogels, cellulose, nitrocellulose, modified cellulose, cross-linked polyvinyl alcohol, cross-linked polyethylene oxide and glycol polymer.

50. The method according to claim 35, wherein in step (d) a plurality of crystallization reactors comprising a plurality of IEF buffers is provided, each IEF buffer

establishing a pH range, wherein at least one IEF buffer establishes a pH range encompassing the pI of the at least biomolecule.

51. The method according to claim 50, wherein the pH range is of no more than 0.2 pH units.

52. The method according to claim 51, wherein the narrow pH range is of no more than 0.02 pH units.

53. The method according to claim 50, wherein the plurality of IEF buffers comprises a polymer.

54. The method according to claim 53, wherein the plurality of IEF buffers having pH ranges that partially overlap.

55. The method according to claim 53, wherein the plurality of IEF buffers having pH ranges that do not overlap.

56. The method according to claim 50, wherein the plurality of crystallization reactors are isolated from one another.

57. The method according to claim 56, wherein the plurality of crystallization reactors are linked, joined, or substantially contiguous to a substrate.

58. The method according to claim 57, wherein the plurality of crystallization reactors are linked, joined, or substantially contiguous with a substrate in a spatially addressable manner.

59. The method according to claim 57, wherein the substrate is biomolecule impermeable.

60. The method according to claim 57, wherein the substrate is ion impermeable.

61. The method according to claim 57, wherein the plurality of crystallization reactors are linked, joined, or substantially contiguous to a substrate in an arrangement selected from the group consisting of: immobilized pH gradient strips, pH membranes and pre-cast gels.

62. The method according to claim 50, wherein the pH step between one or more IEF buffer is no more than 0.1 pH units.

63. The method according to claim 62, wherein the pH step between one or more IEF buffer is no more than 0.02 pH units.

64. An apparatus suitable for inducing rapid formation of biomolecule crystals, comprising:

(a) a buffer chamber having an upper side and a lower side, the lower side being sealed with a bottom such that the buffer chamber encloses at least one buffer compartment capable of holding fluids;

(b) at least one crystallization reactor, the at least one crystallization reactor comprises an IEF buffer, the at least one crystallization reactor is contained within the buffer chamber;

(c) a device for generating an electrical field; and, optionally,

(d) means for circulating fluids contained within the at least one buffer compartment.

65. The apparatus according to claim 64, wherein component (b) is a holder having two ends, an upper side and a lower side, the holder encompasses at least one crystallization reactor, the at least one crystallization reactor comprises an IEF buffer, the holder is contained within the buffer compartment.

66. The apparatus according to claim 64, further comprising two salt bridges having two ends, one end of each salt bridge is in contact with one end of the holder and one end of each salt bridge is contained within the at least one buffer chamber.

67. The apparatus according to claim 66, comprising two buffer chambers, each buffer chamber encloses one end of one salt bridge.

68. The apparatus according to claim 65, wherein the holder is a capillary adapted for comprising at least one crystallization reactor.

69. The apparatus according to claim 64, the apparatus further comprising a temperature-controlled module enabling to manage the temperature at the at least one crystallization reactor.

70. The apparatus according to claim 64, wherein component (b) comprising a holder adapted for supporting a substrate comprising at least one crystallization reactor.

71. The apparatus according to claim 65, wherein the holder encompasses at least one cavity wherein the at least one cavity is adapted for containing a crystallization reactor.

72. The apparatus according to claim 71, wherein the holder has plurality of cavities, such that each cavity is adapted for containing a crystallization reactor.

73. The apparatus according to claim 72, wherein the temperature of one crystallization reactor in a cavity is different from the temperature of another crystallization reactor in another cavity.

74. The apparatus according to claim 64, wherein the buffer chamber comprises a non-conductive material.

75. The apparatus according to claim 65, wherein the holder comprises a material having a larger resistance than that of the polymer comprised within the crystallization reactor.

76. The apparatus according to claim 75, wherein the non-conductive material is selected from the group consisting of: poly-N-methyl methacrylamide, acrylic, lucite, polystyrene, ceramic, glass and poly-methyl-methacrylate.

77. The apparatus according to claim 70, wherein the holder comprises a material that is impermeable to biomolecules.

78. The apparatus according to claim 64, further adapted for detection of the at least one crystallization reactor under a microscope.

79. The apparatus according to claim 64, wherein the device for generating an electrical field comprises a plurality of electrodes.

80. The apparatus according to claim 79, wherein the plurality of electrodes comprises a metal selected from the group consisting of: platinum, titanium, chromium, gold, tantalum, palladium, palladium oxide, germanium, nickel and rhodium or alloys comprising same.

81. The apparatus according to claim 64, wherein the device for generating an electrical field supplies DC or AC currents.

82. The apparatus according to claim 64, wherein the buffer compartment is adapted for holding a solution comprising running buffer and at least one biomolecule dissolved with the running buffer.

83. The apparatus according to claim 64, being miniaturized.

84. The apparatus according to claim 83, further being automated.

85. The apparatus according to claim 64, wherein the biomolecule is selected from the group consisting of: peptides, proteins, polypeptides, enzymes, antibodies, protein-DNA complexes, protein complexes comprising chemical entities, polynucleotides, DNA, RNA, antigens, antigenic epitopes and variants thereof, hormones, carbohydrates, lipids, phospholipids and biotinylated probes.

86. The apparatus according to claim 85, wherein the biomolecule is a protein.

87. The apparatus of claim 64, wherein crystallization occurs within 24 hours, preferably within less than 12 hours.